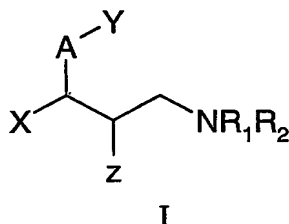


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Claims

1. A compound of formula I:



wherein

A is selected from -O- and -S-;

10 X is selected from C₂-C₈ alkyl, C₂-C₈ alkenyl, C₃-C₈ cycloalkyl and C₄-C₈ cycloalkylalkyl, each of which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, -CF₃, -CN and -CONH₂;

15 Y is selected from phenyl, naphthyl, dihydrobenzothienyl, benzothiazolyl, benzoisothiazolyl, quinolyl, isoquinolyl, naphthyridyl, thienopyridyl, indanyl, 1,3-benzodioxolyl, benzothienyl, indolyl and benzofuranyl, each of which may be optionally substituted with up to 4 or, where possible, 5 substituents each independently selected
 20 from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano; and when Y is indolyl it may be substituted or further substituted by an N-substituent selected from C₁-C₄ alkyl;

Z is selected from H, OR₃ or F, wherein R₃ is selected from H, C₁-C₆ alkyl and phenyl
 25 C₁-C₆ alkyl;

R₁ and R₂ are each independently H or C₁-C₄ alkyl;

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with the proviso that, when Z is H, then Y may not be optionally substituted phenyl or optionally substituted naphthyl.

and pharmaceutically acceptable salts thereof.

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2. A compound as claimed in claim 1, wherein A is -O-.

3. A compound as claimed in claim 1, wherein A is -S-.

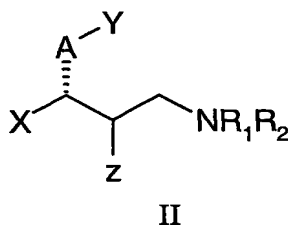
10

4. A compound as claimed in any one of the preceding claims, wherein one of R₁ and R₂ is H.

5. A compounds as claimed in any one of the preceding claims, wherein one of R₁ and R₂ is H and the other is methyl.

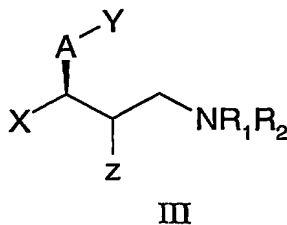
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6. A compound as claimed in any one of the preceding claims, wherein the compound possesses the stereochemistry defined in formula II



20

7. A compound as claimed in any one of claims 1 - 5, wherein the compound possesses the stereochemistry defined in formula III



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8. A compound as claimed in any one of the preceding claims wherein Z is H.

9. A compound as claimed in any one of the preceding claims, wherein X is C₂-C₈ alkyl which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, -CF₃, -CN and -CONH₂.

10. A compound as claimed in claim 9 wherein X is selected from ethyl, n-propyl, i-propyl, n-butyl, i-butyl, n-pentyl, i-pentyl, neopentyl, 3,3-dimethylbutyl and 2-ethylbutyl, each of which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy and -CF₃.

11. A compound as claimed in claim 10 wherein X is selected from n-propyl, i-propyl, n-butyl and i-butyl.

12. A compound as claimed in any one of claims 1 to 8, wherein X is C₂-C₈ alkenyl which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, -CF₃, -CN and -CONH₂.

13. A compound as claimed in claim 12 wherein X is 2-methyl-2-propenyl.

14. A compound as claimed in any one of claims 1 to 8, wherein X is C₄-C₈ cycloalkylalkyl which may be optionally substituted with up to 3 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, -CF₃, -CN and -CONH₂.

15. A compound as claimed in claim 14 wherein X is selected from cyclohexylmethyl and cyclopropylmethyl.

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16. A compound as claimed in any one of the preceding claims, except claim 8, wherein Y is: phenyl optionally substituted with up to 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S-, -CF₃, and -SCF₃.

5

17. A compound as claimed in claim 16, wherein Y is phenyl optionally substituted with up to 2 substituents each independently selected from F, Cl, Br, I, Me, Et, OMe, SMe, -CF₃, and -SCF₃.

10 18. A compound as claimed in any one of claims 1-15, except claim 8, wherein Y is naphthyl optionally substituted with up to 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.

15 19. A compound as claimed in claim 18, wherein Y is unsubstituted naphthyl or naphthyl which is mono-substituted with a substituent selected from halo, C₁-C₄ alkyl and -CF₃.

20 20. A compound as claimed in claim 19 wherein the substituent is located at the 4-position of the naphthyl ring.

21. A compound as claimed in any one of claims 18-20, wherein the point of attachment of the optionally substituted naphthyl group to the -O- or -S- atom is attachment at the 1 position.

25

22. A compound as claimed in any one of the claims 1-15, wherein Y is benzofuranyl, benzothiazolyl, benzoisothiazolyl or indolyl each of which may be optionally substituted with up to 4 or, where possible, 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano; and when Y is indolyl it may be substituted or further substituted by an N-substituent selected from C₁-C₄ alkyl.

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23. A compound as claimed in claim 22, wherein Y is benzofuranyl, benzoisothiazolyl or indolyl each of which may be optionally mono-substituted with Me; and when Y is indolyl it may be substituted or further substituted by an N-methyl substituent.

5 24. A compound as claimed in any one of claims 22-23, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 7 position.

25. A compound as claimed in any one of claims 22-23, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 4 position.

10

26. A compound as claimed in any one of the claims 1-15, wherein Y is benzothienyl optionally substituted with up to 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.

15

27. A compound as claimed in claim 26, wherein Y is benzothienyl optionally substituted with up to 2 substituents each independently selected from halo, C₁-C₄ alkyl, -CF₃ and cyano.

20 28. A compound as claimed in any one of claims 26-27, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 7 position.

29. A compound as claimed in any one of claims 26-27, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 4 position.

25

30. A compound as claimed in any one of claims 26-27, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 5 position.

31. A compound as claimed in any one of claims 26-27, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 6 position.

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32. A compound as claimed in any one of the claims 1-15, wherein Y is quinolyl or isoquinolyl each of which may be optionally substituted with up to 5 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.

5

33. A compound as claimed in claim 32, wherein Y is quinolyl or isoquinolyl each of which may be optionally mono-substituted with a halogen atom.

34. A compound as claimed in claim 32 or 33, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 8 position.

10

35. A compound as claimed in claim 32 or 33, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 5 position.

36. A compound as claimed in any one of the claims 1-15, wherein Y is thienopyridyl which may be optionally substituted with up to 4 substituents each independently selected from halo, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ alkyl-S(O)_n- where n is 0, 1 or 2, nitro, acetyl, -CF₃, -SCF₃ and cyano.

15

37. A compound as claimed in claim 36, wherein Y is unsubstituted thieno-[2,3-b]pyridyl or unsubstituted thieno-[2,3-c]pyridyl.

20

38. A compound as claimed in claim 36 or 37, wherein the point of attachment of the group Y to the -O- or -S- atom is attachment at the 7 position.

25

39. A pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, together with a pharmaceutically acceptable diluent or carrier.

40. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, for use as a pharmaceutical.

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41. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, for use as a selective inhibitor of the reuptake of both serotonin and norepinephrine.

5 42. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, for use in the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.

10 43. A compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, for use in the treatment of a disorder selected from selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flashes/flushes and pain.

15 44. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, in the manufacture of a medicament for selectively inhibiting the reuptake of serotonin and norepinephrine.

20 45. The use of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38, in the manufacture of a medicament for the treatment of a disorder associated with serotonin and norepinephrine dysfunction in mammals.

25 46. The use as claimed in claim 45, wherein the disorder is selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flashes/flushes and pain.

47. The use as claimed in claim 46, wherein the disorder is selected from depression, urinary incontinence and pain.

30 48. The use as claimed in any one of claims 47, wherein the disorder is pain.

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49. A method for selectively inhibiting the reuptake of serotonin and norepinephrine in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38.

5

50. A method for treating disorders associated with serotonin and norepinephrine dysfunction in mammals, comprising administering to a patient in need thereof an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1-38.

10

51. A method as claimed in claim 50, wherein the disorder is selected from depression, OCD, anxiety, memory loss, urinary incontinence, conduct disorders, ADHD, obesity, alcoholism, smoking cessation, hot flashes/flushes and pain.

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52. A method as claimed in claim 51, wherein the disorder is pain.